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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : David Stern, et al.
Serial No. : 08/997,464 Group Art Unit: 1614
Filed : December 23, 1997
: A METHOD FOR EVALUATING THE ABILITY OF A
COMPOUND TO INHIBIT NEUROTOXICITY

1185 Avenue of the Americas
New York, New York 10036
November 10, 1998



Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (Exhibit 1). Copies of the disclosures listed below as items 1-26 are attached hereto as Exhibits 2-27, respectively.

1. Abuchowski, A. et al. (1981) "Immunosuppressive Properties and Circulating Life of Achromobacter Glutaminase-Asparaginase Covalently Attached to Polyethylene Glycol in Man" Cancer Treat. Rep. 65:1077-81 (Exhibit 2);
2. Behl, C., Davis, J. Lesly, R., & Schubert D. (1994) "Hydrogen Peroxide Mediates Amyloid A β Protein Toxicity" Cell 77:817-827 (Exhibit 3);
3. Cotman, C. & Anderson, A. (1995) "A Potential Role for Apoptosis in Neurodegeneration and Alzheimer's Disease" Mol. Neurobiol. 10:19-45 (Exhibit 4);

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4. Cummings, B & Cotman, C. (1995) "Image Analysis of β -amyloid Load in Alzheimer's Disease and Relation to Dementia Severity," Lancet, 346:1524-1428 (Exhibit 5);
5. Dwji, N. And Singer, S. (1996) "Genetic Clues to Alzheimer's Disease," Science 271:159-160 (Exhibit 6);
6. Goedert, M. (1993) "Tau Protein and the Neurofibrillary Pathology of Alzheimer's Disease," Trends Neurosci., 16:460-465 (Exhibit 7);
7. Haas, C. & Selkoe, D. (1994) "Cellular Processing of β -amyloid Precursor Protein and the Genesis of Amyloid β -peptide," Cell, 75:1039-1042 (Exhibit 8);
8. Haas, C. (1996) "Presenile Because of Presenilin: the Presenilin Genes and Early Onset Alzheimer's Disease," Current Opinion in Neurology, 9:254-259 (Exhibit 9);
9. Hardy, J. (1997) "Amyloid, the Presenilins and Alzheimer's Disease," Trends Neurosci., 20:154-159 (Exhibit 10);
10. Hensley, K. et al. (1994) "A Model for β -amyloid Aggregation and Neurotoxicity Based on Free Radical Generation by the Peptide: Relevance to Alzheimer's Disease," Proc. Natl. Acad. Sci. USA 91:3270-3274 (Exhibit 11);
11. Katre, N. V., et al. (1987) "Chemical Modification of Recombinant Interleukin 2 by Polyethylene Glycol Increases Its Potency in the Murine Meth A Sarcoma Model," Proc. Natl. Acad. Sci. USA, 84:1487-91 (Exhibit 12);
12. Koh, J. Y., et al. (1990) "Beta-amyloid Protein Increases the Vulnerability of Cultured Cortical Neurons to Excitotoxic Damage," Brain Res., 533:315-320 (Exhibit 13);

13. Koo, E.H., et al. (1993) "Amyloid Beta-Protein As a Substrate Interacts with Extracellular Matrix to Promote Neurite Outgrowth," Proc. Natl. Acad. Sci. USA, 90:4748-4752 (Exhibit 14);
14. Kosik, K. (1994) "Alzheimer's Disease Sphinx: A Riddle with Plaques and Tangles," J. Cell Biol. 127:1501-1504 (Exhibit 15);
15. Loo, D. T., et al. (1993) "Apoptosis Is Induced by Beta-Amyloid in Cultured Central Nervous System Neurons," Proc. Natl. Acad. Sci. USA, 90:7951-7955 (Exhibit 16);
16. Mattson, M.P. (1995) "Free Radicals and Disruption of Neuronal Ion Homeostasis in Alzheimer's Disease: A Role for Amyloid beta-peptide?" Neurobiol. Aging 16:661-674 (Exhibit 17);
17. Meda, L., et al. (1995) "Activation of Microglial Cells by Beta-Amyloid Protein and Interferon-Gamma," Nature, 374:647-650 (Exhibit 18);
18. Pike, C. J., et al. (1993) "Neurodegeneration Induced by Beta-Amyloid Peptides in Vitro: the Role of Peptide Assembly State," J. Neurosci. 13:1676-1687 (Exhibit 19);
19. Tanzi, R., et al. (1996) "The Gene Defects Responsible For Familial Alzheimer's Disease," Neurobiol. Dis. 3:159-168 (Exhibit 20);
20. Trojanowski, J. and Lee, V. (1994) "Paired Helical Filament Tau In Alzheimer's Disease, The Knase Connection," Am. J. Pathol., 144: 449-453 (Exhibit 21);

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21. Wolozin, B., et al. (1996) "Participation of PS2 In Apoptosis: Enhanced Basal Activity Conferred By An Alzheimer Mutation," Science, 274:1710-1713 (Exhibit 22);
22. Yan, S. D., et al. (1997) "Amyloid- β Peptide RAGE Interaction Elicits Neuronal Expression of M-CSF: A Proinflammatory Pathway In Alzheimer's Disease," Proc. Natl. Acad. Sci. USA, 94: 5296-5301 (Exhibit 23);
23. Yan, S. D., et al. (1996) "RAGE And Amyloid-A β Peptide Neurotoxicity In Alzheimer's Disease," Nature, 382:685-691 (Exhibit 24);
24. Yankner, B., et al. (1990) "Neurotrophic And Neurotoxic Effects Of Amyloid β -Protein: Reversal By Tachykinin Neuropeptides," Science, 250:279-282 (Exhibit 25);
25. Yankner, B. (1996) "Mechanisms Of Neuronal Degeneration As In Alzheimer's Disease," Neuron, 16:921-932 (Exhibit 26);
26. Younkin, S. (1995) "Evidence That A β is The Real Culprit In Alzheimer's Disease," Ann. Neurol., 37:287-288 (Exhibit 27);

Applicants request that the Examiner review the references and make them of record in the subject application.

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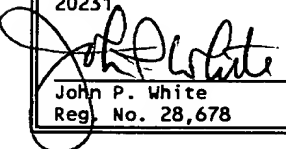
No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. If any such fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231



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11/10/98
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